

REMARKS

The present application was filed on March 27, 2001 (claiming priority from United States Provisional Application Number 60/245,396, filed November 2, 2000) with claims 1-43. Claims 7-21, 28-32 and 39-43 have been withdrawn from consideration in response to a restriction requirement and claims 4, 25 and 36 have been withdrawn from consideration in response to a species election. Therefore, claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 are presented herein for examination on the merits. Applicant acknowledges that while claims 4, 7-21, 25, 28-32, 36 and 39-43 have been withdrawn from consideration, as highlighted above, these claims are still pending in the present application.

Independent claims 1, 22 and 33 are amended herein. No new matter is being introduced by these amendments. Support for the amendment to independent claims 1, 22 and 33 may be found, for example, on page 6, lines 13-15, and on page 9, lines 5-8, of the specification.

In the outstanding Office Action, the Examiner rejected claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The Examiner further rejected claims 1-3, 5 and 6 under 35 U.S.C. §101 as allegedly drawn to non-statutory subject matter. The Examiner rejected claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. The Examiner rejected claim 1 under 35 U.S.C. §102(b) as allegedly unpatentable over Bar-Or et al., Database CaPlus, DN 103:84898, Archives of Microbiology (1985), 142(1), pages 21-27 (hereinafter "Bar-Or"). The Examiner also rejected claim 1 under 35 U.S.C. §102(b) as allegedly unpatentable over J. L. Cornette et al., *Hydrophobicity Scales and Computational Techniques for Detecting Amphipathic Structures in Proteins*, J. MOL. BIOL. 195, pgs. 659-685 (1987) (hereinafter "Cornette"). The Examiner also objected to the specification as containing an embedded hyperlink and/or other form of browser-executable code.

The present invention has been described in Applicant's prior response, incorporated by reference herein.

FORMAL REJECTIONS

As mentioned above, the Examiner finally rejected claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

5 Specifically, the Examiner stated, with regard to independent claim 1, that the claim is “indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble.” See, Office Action, beginning on page 2, 4th paragraph. Specifically, the Examiner stated that the “claim does not set forth the conditions when determining/shifting of hydrophobicity distribution results in ‘spatioially (sic.) profiling
10 proteins.’” See *Id.* Applicants respectfully disagree with the Examiner’s assertions.

Applicants submit that the steps of determining a hydrophobicity distribution for a protein and shifting the hydrophobicity distribution, as recited in independent claim 1, “agree[] back with the preamble” of that claim, as these are steps performed in spatially profiling a protein. By way of example only, Applicants point to page 9, lines 4-5, of the specification
15 wherein it is explained that the hydrophobicity distribution results from the spatial distribution of the amino acid residues in a protein. Thus, the shifted hydrophobicity distribution of a protein, as in independent claim 1, is associated with the spatial profile of the protein.

The Examiner further stated in the Office Action, page 3, 1st paragraph, that “the preamble addresses spatially profiling plurality of proteins while the main body of the claim
20 addresses a single protein.” Applicants respectfully traverse the examiner’s rejection. Notwithstanding this traversal, Applicants have amended independent claim 1.

The Examiner further found the step of determining a hydrophobicity distribution of a protein to be vague and indefinite. The Examiner stated on page 3, 4th paragraph, that,

25 Applicant explains that the hydrophobicity distribution is determined from the spatial distribution of amino acid residues. This may explain the term hydrophobicity distribution of amino acid residues in protein, but not the ‘hydrophobicity distribution of a protein’ as used in the claims.

Applicants respectfully resubmit that one of ordinary skill in the art would be able
30 to equate the term “hydrophobicity distribution of a protein” with, for example, the term

“hydrophobicity distribution of amino acid residues in a protein,” given the teachings of the present supporting specification. For example, Applicants again point to the teachings in the specification wherein the hydrophobicity distribution arises from the spatial distribution of the residues and their assigned values of hydrophobicity. See, for example, page 9, lines 1-5 of the specification and FIG. 2.

Applicants also again point out that the alleged discrepancy between the terms “hydrophobicity distribution of amino acid residues in a protein” (as set forth by the Examiner, see above) and “the hydrophobicity distribution of a protein” (as recited, e.g., in claims 1, 22 and 33) is a mere matter of preference. The Examiner is reminded that the “focus during examination of claims for compliance with the requirement for definiteness of 35 U.S.C. 112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available. . . . [Claims should be allowed] which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire.” M.P.E.P. §2173.02 (emphasis in original)

Comments of the Examiner in the present and in past Actions support Applicant’s position that these terms would be recognizable as being synonymous by one of ordinary skill in the art. Thus, regardless of whether the terms used in the claims are the best terms in the opinion of the Examiner, as long as they are properly supported and defined in the specification, and understandable by one of ordinary skill in the art, the claims should be allowable.

The Examiner further stated on page 3, 4th paragraph, of the Office Action that, “the section in the specification addressed by applicant, describes values of hydrophobicity of amino acid residues lying within certain surface (sic.), not ‘hydrophobicity distribution of a protein.’” Again, Applicants point out that it appears the Examiner is referring to Applicant’s prior reference to page 9, lines 1-5 of the specification. Namely, the paragraph spanning pages 8 and 9 of the specification (beginning on page 8, line 26) recites that an ellipsoidal surface is obtained and the values of hydrophobicity for amino acid residues lying within this surface are collected. This teaching is directed to spatially profiling the hydrophobicity distribution of

amino acid residues in a protein using second-order moments. See, for example, page 8, lines 6-7 of the specification.

What Applicant in fact intended in making reference to page 9, lines 1-5 of the specification and FIG. 2 was simply that assigning values of hydrophobicity for the amino acid residues making up a protein may be based on consensus hydrophobicity values, such as those shown in FIG. 2. For example, the specification beginning on page 6, line 25, sets forth that the hydrophobicity distribution is determined wherein each amino acid residue is assigned a hydrophobicity consensus value, e.g., based on the representative hydrophobicity value table shown in FIG. 2.

The above remarks were presented in Applicant's previous response. However, the present Action is silent as to these remarks.

The Examiner further stated on page 4, 1st paragraph, of the Office Action, that even only the limited '*in silico*' meaning of the term intended by applicant is addressed, it is still unclear whether the term 'hydrophobicity distribution of a protein' encompasses distribution of hydrophobicity values of individual residues throughout the protein, distribution of hydrophobicity on the surface (or in the core) of the protein, or general vector/matrix indicating distribution of hydrophobicity.

Applicant respectfully disagrees with the Examiner's assertions and respectfully submits that the term "hydrophobicity of a protein" is not unclear, given the teachings of the claims and supporting specification. Namely, on page 6, lines 25 -26, of the specification, it is taught that the hydrophobicity distribution of a protein(s) is based on each amino acid residue being assigned a hydrophobicity consensus value. Thus, according to the present teachings, the hydrophobicity distribution is based on the hydrophobicities of the amino acids that make up the protein.

Given the above remarks, it is thus Applicant's position that one of ordinary skill in the art would be able to ascertain the metes and bounds of the present claims from the teachings of the specification. Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection.

As further highlighted above, the Examiner rejected claims 1-3, 5 and 6 under 35 U.S.C. §101 as allegedly drawn to non-statutory subject matter. Specifically, the Examiner stated beginning on page 5, 1st paragraph of the Office Action that,

[t]he invention as claimed is drawn to a series of computational steps towards modifying hydrophobicity values of amino acid constituents of a protein in a modeled virtual environment. The specification discloses mathematical steps used in the method. These steps result in a protein model having zero net hydrophobicity in the virtual environment. A process consisting solely of mathematical operates, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus can not constitute a statutory process. There is no “useful, concrete, and tangible result” obtained as a result of the claimed method. Applicant states that the ‘shifted hydrophobicity distribution’ may be used for comparing ‘hydrophobic ratios’, but no ‘useful, concrete, and tangible result’ for said ‘ratios’ is identified either.

Applicant respectfully disagrees with the Examiner’s assertions. First, as Applicant previously pointed out, independent claim 1, from which claims 2, 3, 5 and 6 ultimately depend, is expressly directed to a practical method for “spatially profiling proteins.” Thus, these claims are clearly tied to a practical application. A process that is limited to a practical application of an abstract idea or mathematical algorithm in the technological arts is patentable. See Examination Guidelines for Computer-Related Inventions, § IV. B. 2. b. (ii). In any event, the analysis does not stop there. The Supreme Court has stated that the “[t]ransformation and reduction of an article ‘to a different state or thing’ is the clue to patentability of a process claim.” *Gottshalk v. Benson*, 409 U.S. 63, 70, 175 U.S.P.Q. (BNA) 676 (1972). In other words, claims that require some kind of transformation of subject matter, which has been held to include intangible subject matter, such as data or signals, that are representative of or constitute physical activity or objects have been held to comply with § 101. See, for example, *In re Warmerdam*, 31 U.S.P.Q.2d (BNA) 1754, 1759 n.5 (Fed. Cir. 1994) or *In re Schrader*, 22 F.3d 290, 295, 30 U.S.P.Q.2d (BNA) 1455, 1459 n.12 (Fed. Cir. 1994). Thus, as expressly set forth in independent claim 1, a hydrophobicity distribution of a protein is determined. The hydrophobicity distribution is then *transformed* by being shifted.

Further, Applicant maintains that the shifted hydrophobicity distribution of a protein, as claimed, e.g., in independent claim 1, is a useful, concrete and tangible result.

Specifically, as clearly taught in the specification, for example, beginning on page 4, line 26, the shifted hydrophobicity distribution provides a basis for comparing proteins. By way of example only, it is stated on page 5, lines 1-2 that “without shifting the hydrophobicity distribution, the ability to compare different proteins is significantly degraded.”

5 With regard to the hydrophobic ratios, Applicant asserts that the ratios are a ‘useful, concrete, and tangible result.’ Namely, as set forth, for example, beginning on page 5, line 15, of the specification, it is provided that, e.g., globular proteins can be distinguished from other proteins or decoys by determining a ratio of the distance at which the adjusted second-order moment of hydrophobicity vanishes and the distance at which the adjusted zero-order
10 moment of hydrophobicity vanishes (or vice versa).

 Given the above remarks, Applicant respectfully submits that claims 1-3, 5 and 6 fully comport with the requirements of 35 U.S.C. §101 and as such, Applicant respectfully requests reconsideration and withdrawal of the rejections.

 As mentioned above, the Examiner also rejected claims 1-3, 5, 6, 22-24, 26, 27,
15 33-35, 37 and 38 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Specifically, on page 6, 1st paragraph, of the Office Action, the Examiner stated that,

 [t]he specification appears to disclose a . . . method wherein
20 hydrophobicity of amino acid residues comprising the protein of interest are shifted by subtracting the average hydrophobicity from each value of hydrophobicity distribution of each amino acid residue, so that as a result the net hydrophobicity of protein vanishes. The specification appears to indicate that applicant’s inventive concept revolves around such specific ‘shifting’ operation, rather than encompasses any broad definition of the term ‘shifting.’ This is not reflected in the claims.

25 Applicant respectfully traverses the Examiner’s rejection. Notwithstanding this traversal however, Applicant has amended independent claim 1 (from which claims 2-3, 5 and 6 depend), independent claim 22 (from which claims 23, 24, 26 and 27 depend) and independent claim 33 (from which claims 34, 35, 37 and 38 depend). As such, Applicant respectfully
30 requests reconsideration and withdrawal of the rejections.

 As mentioned above, the Examiner also objected to the specification as containing an embedded hyperlink and/or other form of browser-executable code. Applicant has amended

the specification at page 17, lines 7-8, to remove the web site address appearing therein. Reconsideration and withdrawal of the rejection is thus respectfully requested.

PRIOR ART REJECTIONS

5 As mentioned above, the Examiner rejected claim 1 under 35 U.S.C. §102(b) as allegedly unpatentable over Bar-Or. On page 8, 3rd paragraph, of the Office Action, the Examiner stated that Bar-Or “includes initial evaluation of hydrophobicity, which reads on instantly claimed step of ‘determining a hydrophobicity distribution’, and a step of treatment of cell surface which clearly shifts hydrophobicity distribution of a protein (e.g., as a result of
10 treatment with a proteolytic agent).”

Applicant respectfully traverses the Examiner’s rejections. However, notwithstanding this traversal, Applicant has amended independent claim 1. Applicant further points out that Bar-Or does not teach or suggest either determining a hydrophobicity distribution of a protein. Namely, Bar-Or makes no mention of the hydrophobicity of any given protein. The
15 techniques mentioned in Bar-Or are directed to shifting cell surface hydrophobicity. The distribution of hydrophobicity in a protein is not taught in Bar-Or.

As such, Applicant respectfully requests reconsideration and withdrawal of the rejection of independent claim 1 over Bar-Or.

As mentioned above, the Examiner also rejected claim 1 under 35 U.S.C. §102(b)
20 as allegedly unpatentable over Cornette. On page 8, 5th paragraph, of the Office Action, the Examiner stated that,

Cornette teaches calculation of hydrophobic moment for each residue (i.e., determining ‘hydrophobicity distribution’) and plotting them on a graph. For comparative purposes, to compare different approaches, the
25 hydrophobicity values are normalized to have a value of 1000 at the frequency angle of 100° (i.e., ‘hydrophobicity distribution’ is ‘shifted’).

Applicant respectfully traverses the Examiner’s rejections. However, notwithstanding this traversal, Applicant has amended independent claim 1. As such, Applicants
30 respectfully requests reconsideration and withdrawal of the rejection of independent claim 1 over Cornette.

In view of the foregoing, the invention, as claimed in claim 1, cannot be said to be taught or suggested by Bar-Or or Cornette. Accordingly, Applicant submits that all claims presented here for examination, i.e., claims 1-3, 5, 6, 22-24, 26, 27, 33-35, 37 and 38, are in condition for allowance and such favorable action is earnestly solicited.

5 If any outstanding issues remain, or if the Examiner has any further suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

10 Respectfully submitted,



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